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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,860	10/19/2005	Marc K. Hellerstein	416272003600	5469

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

MAIL DATE	DELIVERY MODE
05/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,860	HELLERSTEIN, MARC K.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,23,24,26 and 27* is/are pending in the application.

4a) Of the above claim(s) *14-20,23,24,26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response and amendment filed March 21, 2008 is acknowledged and entered. Claims 1-20, 23, 24, 26 and 27 are pending. Claims 14-20, 23, 24, 26 and 27 are withdrawn from consideration being drawn to non-elected subject matter. Claims 1-13 remain under examination.

2. The rejection of claims 1-13 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of Applicant's persuasive arguments.

Claims Summary

3. The claims as amended are drawn to a method of determining the rate of replication (growth) or destruction (death) of an infectious agent while they are in a host organism. The method allows the *in vivo* assessment of microbial growth (see specification page 6, first full paragraph, last sentence). The method steps include, but are not limited to the following:

a. Administering an isotope-labeled precursor molecule to the host to allow the molecule to become incorporated into a biochemical component of the infectious agent in the host;
b. Obtaining a sample(s) from the host that comprises the biochemical component of the infectious agent;
c. Separating the biochemical component of the infectious agent from the sample(s);
d. Measuring isotopic content, rate of change of isotopic content, and/or pattern or rate of change of pattern of said isotopic content in the biochemical component; and
e. Calculating rate of synthesis or breakdown of the biochemical component to determine the rate of replication or destruction of the infectious agent in the host.

Specifically, the sample is a tissue or bodily fluid, such as urine, blood, saliva, etc., see the list in claim 13. The host organism is a mammal, including humans. The infectious agent is any of bacteria, viruses (HIV, HBV, HCV, or other clinically important virus), protozoa, yeast and parasites. The precursor molecule is any molecule utilized in one or more specific biochemical pathways to produce a biochemical component of an infectious agent (page 10, first full paragraph). Examples of isotope-labeled precursor molecules are $^{2}H_20$, ^{2}H-glucose, ^{2}H-labeled amino acids, etc. The biochemical component is a constituent part of an infectious agent that is synthesized from precursor molecules, such as DNA, RNA, proteins, lipids, carbohydrates or porphyrins (page 10, second full paragraph). The isotopic label is selected from the group consisting of ^{13}C, ^{14}C, ^{2}H, ^{3}H, ^{15}N, ^{35}S, ^{11}C and ^{35}P. Measurement of isotopic content is performed via mass spectrometry.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-13 remain rejected under 35 U.S.C. 102(b) as being anticipated by Hellerstein (US Patent 6,010,846, "Hellerstein"). The claims are summarized above. Hellerstein discloses a method for measuring cellular proliferation and destruction rates using isotope labels (abstract). Column 4, lines 17-26 is reproduced below:

> In another aspect of the invention, methods for measuring the rates of proliferation and/or destruction of T cells in a subject infected with human immunodeficiency virus (HIV) are provided. Such methods comprise administering a detectable amount of a stable isotope label to the subject, wherein the label is incorporated into DNA of the T cells of the subject via the de novo nucleotide synthesis pathway. The label in the DNA of the T cells of the subject is detected to measure the rates of proliferation and/or destruction of T cells in the subject.

The isotope-labeled precursor molecules are administered to human subjects (col. 13, section 5.3.2). For example, ^{2}H-glucose (precursor of deoxyribose) is administered to an HIV-infected subject and the label is incorporated into the subject's DNA to measure cellular proliferation/destruction. Although Hellerstein's disclosure does not teach that the ^{2}H-glucose is a precursor of the deoxyribose that is incorporated into the proviral DNA of HIV, this is expected. Since Hellerstein suggests the administration of ^{2}H-glucose to HIV-infected patients, Hellerstein's patient population and the patient population on the instantly claimed methods are the same. By performing Hellerstein's method for the *in vivo* assessment of T cell proliferation/destruction, one would also inherently be performing the instantly claimed method because the extraction of DNA from T cells is expected to also extract DNA from HIV proviral DNA in infected T cells. Hellerstein's separation of T cells (containing HIV DNA) from blood (biological sample) meets the claim limitation represented in step c) of the claims. The mass spectrometry step disclosed in Hellerstein (see claims) for the purpose of tracking rates of T cell proliferation/destruction is expected to also track the rate of HIV proliferation/destruction. Therefore, the method as claimed is anticipated by Hellerstein.

Applicant's arguments have been carefully considered but fail to persuade. Applicant argues that the separation step c) in the claims is not taught by Hellerstein. Applicant points to example 6.2.5 of Hellerstein which teaches non-separation of the biochemical component of the

infectious agent from the biochemical component of the host prior to analysis by mass spectrometry. Applicant argues that total DNA, both viral and human (from the T cells) was recovered and analyzed. Applicant points out that the instant invention, in one embodiment, isolates HIV from human blood plasma by ultracentrifugation, followed by electrophoresis to isolate viral-specific proteins; mass spec is then performed on the viral specific proteins.

In response to Applicant's arguments, the Office recognizes the difference between Hellerstein's teachings and Applicant's *intended* invention. However, the claim language does not reflect the intent. The instant claim language does not recite anything about separating viral DNA from cellular DNA. The claims simply state that the "biochemical component of said infectious agent" is separated from the sample. The sample is not limited to any particular component. For example, in claim 2, the sample is tissue; in claim 3, the sample is bodily fluid. These limitations do not require separation of viral DNA (or any other pathogen's DNA) from cellular DNA, which is why Hellerstein's separation of T cells (containing both viral and host DNA) from blood (bodily fluid) meets the limitation of step c) in the instant claims. Therefore, the claims *as written* remain anticipated by Hellerstein's disclosure.

Conclusion

5. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30), alternate Fridays off,. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/ 5-21-08
Primary Examiner, TC1600